

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (previously presented): A method for estimating a virtual patient's fasting plasma glucose (FPG) level, comprising:

- determining the virtual patient's basal hepatic production (FPG_0);
- determining the virtual patient's insulin level (I);
- calculating the virtual patient's FPG at time t by solving an equation

$$FPG(t) = FPG_0 / (I * E), \text{ wherein } E \text{ is a value representing efficiency of insulin use; and}$$

outputting at least one value for the virtual patient's FPG at time t to a user.

Claim 2 (previously presented): The method of claim 1, wherein E is scaled such that $E = 1$ in the absence of diabetes and $0 \leq E < 1$ in the presence of diabetes.

Claim 3 (currently amended): The method of claim 1, wherein for type 2 diabetes, an equation representing E is:

$$E(DF_2) = \left(a + b / \left(1 + (DF_2 / c)^d \right) \right)^{\frac{1}{2}}, \text{ wherein the parameters } a, b, c, \text{ and } d \text{ are set to fit data for } E \text{ and } DF_2 \text{ for a population that is represented by the virtual patient, and } DF_2 \text{ is a type 2 diabetes feature that represents an incidence of type 2 diabetes for the virtual patient, so that values of } DF_2 \text{ above a threshold value correspond to an occurrence of type 2 diabetes in the virtual patient.}$$

Claim 4 (currently amended): The method of claim 3, wherein

$$DF_2(t) = \left(1 - \exp \left(-a_1 * IGT(\xi_3) / \left(1 + \exp \left(-\frac{(t - b_1)}{c_1} \right) \right) \right) \right) * RBMI(BMI) / \xi_2, \text{ wherein } \xi_2 \text{ and } \xi_3$$

are random values selected from distributions for randomizing the virtual patient within the population, IGT is an impaired glucose tolerance value indexed by the random value ξ_3 , $RBMI$ is a relative risk associated with the virtual patient's body mass index (BMI), and the parameters a_1 ,

b_1 , and c_1 , are set to fit data for DF_2 and t for the population that is represented by the virtual patient.

Claim 5 (currently amended): The method of claim 4, wherein the *RBMI* is represented by:

$$RBMI(BMI) = a_2 + b_2 / \left(1 + e^{-(RBMI - c_2) / d_2} \right), \text{ and the parameters } a_2, b_2, c_2, \text{ and } d_2, \text{ are set to}$$

fit data for $RBMI$ and BMI for the population that is represented by the virtual patient.

Claim 6 (previously presented): The method of claim 4, wherein *IGT* is represented by:

$$IGT(\xi_3) = 2(1 - \xi_3)$$

wherein the random value ξ_3 is designed so that the occurrence of diabetes corresponds to variations that occur in the population that is represented by the virtual patient.

Claim 7 (currently amended): The method of claim 1, wherein said determining said virtual patient's basal hepatic production in type 2 diabetes includes solving an equation $FPG_0(t) = G(t) * H(DF_2(t))$, wherein $G(t)$ represent a basal production in people who do not have diabetes, H represents a degree of insulin resistance in a person with diabetes, and DF_2 ~~is a type 2 diabetes feature that~~ represents an incidence of type 2 diabetes for the virtual patient, so that values of DF_2 above a threshold value correspond to an occurrence of type 2 diabetes in the virtual patient.

Claim 8 (currently amended): The method of claim 7, wherein

$$H(DF_2(t)) = 1 / \left(MAX \left[E^2(DF_2(t+a)), b \right] \right), \text{ and the parameters } a \text{ and } b \text{ are set to fit data for } H \text{ and } DF_2 \text{ for a population that is represented by the virtual patient.}$$

Claim 9 (currently amended): The method of claim 7, wherein

$$G(t) = (a + bt^{1.5} - c * t^3 + \Delta_g) / (d - e \exp(-DF_2(t)\xi_2)), \text{ wherein } \Delta_g \text{ represents a variance of}$$

basal hepatic production across individuals, the parameters a , b , c , d , and e are set to fit data for G and t for a population that is represented by the virtual patient, and ξ_2 is a random value selected from a distribution for randomizing the virtual patient within the population.

Claim 10 (currently amended): The method of claim 1, wherein

$I(DF_1, DF_2) = H(DF_2) * E(DF_2) / (1 + \exp((DF_1 - a)/b))$, and wherein DF_1 is a ~~type 1 diabetes feature that~~ represents an incidence of type 1 diabetes for the virtual patient so that values of DF_1 above a first threshold value correspond to an occurrence of type 1 diabetes in the virtual patient, DF_2 is a ~~type 2 diabetes feature that~~ represents an incidence of type 2 diabetes for the virtual patient so that values of DF_2 above a second threshold value correspond to an occurrence of type 2 diabetes in the virtual patient, H represents a degree of insulin resistance in a person with diabetes, and the parameters a and b are set to fit data for I , DF_1 and DF_2 for a population that is represented by the virtual patient.

Claims 11-30 (canceled).

Claim 31 (previously presented): An apparatus for estimating a virtual patient's fasting plasma glucose (FPG) level, the apparatus comprising:

means for determining the virtual patient's basal hepatic production (FPG_0);

means for determining the virtual patient's insulin level (I);

means for calculating the virtual patient's FPG at time t by solving an equation

$$FPG(t) = FPG_0 / (I * E), \text{ wherein } E \text{ is a value representing efficiency of insulin use; and}$$

means for outputting at least one value for the virtual patient's FPG at time t to a user.

Claim 32 (previously presented): The apparatus of claim 31, wherein E is scaled such that $E = 1$ in the absence of diabetes and $0 \leq E < 1$ in the presence of diabetes.

Claim 33 (currently amended): The apparatus of claim 31, wherein for type 2 diabetes, an equation representing E is:

$$E(DF_2) = \left(a + b / \left(1 + (DF_2 / c)^d \right) \right)^{\frac{1}{2}}, \text{ wherein the parameters } a, b, c, \text{ and } d \text{ are set to fit}$$

data for E and DF_2 for a population that is represented by the virtual patient, and DF_2 is a ~~type 2 diabetes feature that~~ represents an incidence of type 2 diabetes for the virtual patient, so that values of DF_2 above a threshold value correspond to an occurrence of type 2 diabetes in the virtual patient.

Claim 34 (currently amended): The apparatus of claim 33, wherein

$$DF_2(t) = \left(1 - \exp \left(-a_1 * IGT(\xi_3) / \left(1 + \exp \left(-\frac{(t-b_1)}{c_1} \right) \right) \right) \right) * RBMI(BMI) / \xi_2, \text{ wherein } \xi_2 \text{ and } \xi_3$$

are random values selected from distributions for randomizing the virtual patient within the population, IGT is an impaired glucose tolerance value indexed by the random value ξ_3 , $RBMI$ is a relative risk associated with the virtual patient's body mass index (BMI), and the parameters a_1 , b_1 , and c_1 , are set to fit data for DF_2 and t for the population that is represented by the virtual patient.

Claim 35 (currently amended): The apparatus of claim 33, wherein the $RBMI$ is represented by:

$$RBMI(BMI) = a_2 + b_2 / \left(1 + e^{-(BMI-c_2)/d_2} \right), \text{ and the parameters } a_2, b_2, c_2, \text{ and } d_2, \text{ are set to}$$

fit data for $RBMI$ and BMI for the population that is represented by the virtual patient.

Claim 36 (previously presented): The apparatus of claim 34, wherein IGT is represented by:

$$IGT(\xi_3) = 2(1 - \xi_3),$$

wherein the random value ξ_3 is designed so that the occurrence of diabetes corresponds to variations that occur in the population that is represented by the virtual patient.

Claim 37 (currently amended): The apparatus of claim 31, wherein said means for determining said virtual patient's basal hepatic production in type 2 diabetes includes means for solving an equation $FPG_0(t) = G(t) * H(DF_2(t))$, wherein $G(t)$ represent a basal production in people who do not have diabetes, H represents a degree of insulin resistance in a person with diabetes, and DF_2 is a ~~type 2 diabetes feature that~~ represents an incidence of type 2 diabetes for the virtual patient, so that values of DF_2 above a threshold value correspond to an occurrence of type 2 diabetes in the virtual patient.

Claim 38 (currently amended): The apparatus of claim 37, wherein

$$H(DF_2(t)) = 1 / \left(MAX \left[E^2(DF_2(t+a)), b \right] \right), \text{ and the parameters } a \text{ and } b \text{ are set to fit data for } H \text{ and } DF_2 \text{ for a population that is represented by the virtual patient.}$$

Claim 39 (currently amended): The apparatus of claim 37, wherein

$G(t) = (a + bt^{1.5} - c * t^3 + \Delta_g) / (d - e \exp(-DF_2(t)\xi_2))$, wherein Δ_g represents a variance of basal hepatic production across individuals, the parameters a, b, c, d, and e are set to fit data for G and t for a population that is represented by the virtual patient, and ξ_2 is a random value selected from a distribution for randomizing the virtual patient within the population.

Claim 40 (currently amended): The apparatus of claim 31, wherein

$I(DF_1, DF_2) = H(DF_2) * E(DF_2) / (1 + \exp((DF_1 - a)/b))$, and wherein DF_1 is a ~~type 1 diabetes feature that~~ represents an incidence of type 1 diabetes for the virtual patient so that values of DF_1 above a first threshold value correspond to an occurrence of type 1 diabetes in the virtual patient, DF_2 is a ~~type 2 diabetes feature that~~ represents an incidence of type 2 diabetes for the virtual patient so that values of DF_2 above a second threshold value correspond to an occurrence of type 2 diabetes in the virtual patient, H represents a degree of insulin resistance in a person with diabetes, and the parameters a and b are set to fit data for I, DF_1 and DF_2 for a population that is represented by the virtual patient.

Claims 41-51 (canceled).

Claim 52 (previously presented): A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating a virtual patient's fasting plasma glucose (FPG) level, the method comprising:

- determining the virtual patient's basal hepatic production (FPG_0);
- determining the virtual patient's insulin level (I);
- calculating the virtual patient's FPG at time t by solving an equation

$$FPG(t) = FPG_0 / (I * E), \text{ wherein } E \text{ is a value representing efficiency of insulin}$$

use; and

outputting at least one value for the virtual patient's FPG at time t to a user.

Claims 53-60 (canceled).

Claim 61 (previously presented): The method of claim 1, wherein the at least one value based on the virtual patient's FPG at time t is saved in at least one file in a computer storage device.

Claim 62 (previously presented): The method of claim 3, further comprising:

setting values for the parameters a, b, c, and d by fitting the equation representing E to data for the population according to a least-squares criterion.

Claim 63 (previously presented): The apparatus of claim 31, wherein the at least one value based on the virtual patient's FPG at time t is saved to a computer-readable medium.

Claim 64 (previously presented): The apparatus of claim 33, further comprising:

means for setting values for the parameters a, b, c, and d by fitting the equation representing E to data for the population according to a least-squares criterion.

Claim 65 (previously presented): The program storage device of claim 52, wherein E is scaled such that $E = 1$ in the absence of diabetes and $0 \leq E < 1$ in the presence of diabetes.

Claim 66 (currently amended): The program storage device of claim 52, wherein for type 2 diabetes, an equation representing E is:

$$E(DF_2) = \left(a + b / \left(1 + (DF_2 / c)^d \right) \right)^{\frac{1}{2}}, \text{ wherein the parameters a, b, c, and d are set to fit}$$

data for E and DF_2 for a population that is represented by the virtual patient, and ~~DF_2 is a type 2 diabetes feature that~~ represents an incidence of type 2 diabetes for the virtual patient, so that values of DF_2 above a threshold value correspond to an occurrence of type 2 diabetes in the virtual patient.

Claim 67 (currently amended): The program storage device of claim 66, wherein

$$DF_2(t) = \left(1 - \exp \left(-a_1 * IGT(\xi_2) / \left(1 + \exp \left(-\frac{(t-b_1)}{c_1} \right) \right) \right) \right) * RBMI(BMI) / \xi_2, \text{ wherein } \xi_2 \text{ and } \xi_3$$

are random values selected from distributions for randomizing the virtual patient within the population, IGT is an impaired glucose tolerance value indexed by the random value ξ_3 , RBMI is a relative risk associated with the virtual patient's body mass index (BMI), and the parameters a_1 , b_1 , and c_1 , are set to fit data for DF_2 and t for the population that is represented by the virtual patient.

Claim 68 (currently amended): The program storage device of claim 67, wherein the *RBMI* is represented by:

$$RBMI(BMI) = a_2 + b_2 / \left(1 + e^{-(BMI - c_2)/d_2} \right), \text{ and the parameters } a_2, b_2, c_2, \text{ and } d_2, \text{ are set to fit data for RBMI and BMI for the population that is represented by the virtual patient.}$$

Claim 69 (previously presented): The program storage device of claim 67, wherein *IGT* is represented by:

$$IGT(\xi_3) = 2(1 - \xi_3)$$

wherein the random value ξ_3 is designed so that the occurrence of diabetes corresponds to variations that occur in the population that is represented by the virtual patient.

Claim 70 (currently amended): The program storage device of claim 52, wherein said determining said virtual patient's basal hepatic production in type 2 diabetes includes solving an equation $FPG_0(t) = G(t) * H(DF_2(t))$, wherein $G(t)$ represent a basal production in people who do not have diabetes, H represents a degree of insulin resistance in a person with diabetes, and DF_2 is a type 2 diabetes feature that represents an incidence of type 2 diabetes for the virtual patient, so that values of DF_2 above a threshold value correspond to an occurrence of type 2 diabetes in the virtual patient.

Claim 71 (currently amended): The program storage device of claim 70, wherein

$$H(DF_2(t)) = 1 / \left(\text{MAX} \left[E^2(DF_2(t+a)), b \right] \right), \text{ and the parameters } a \text{ and } b \text{ are set to fit data for H and } DF_2 \text{ for a population that is represented by the virtual patient.}$$

Claim 72 (currently amended): The program storage device of claim 70, wherein

$$G(t) = (a + bt^{1.5} - c * t^3 + \Delta_g) / (d - e \exp(-DF_2(t)\xi_2)), \text{ wherein } \Delta_g \text{ represents a variance of basal hepatic production across individuals, the parameters } a, b, c, d, \text{ and } e \text{ are set to fit data for G and t for a population that is represented by the virtual patient, and } \xi_2 \text{ is a random value selected from a distribution for randomizing the virtual patient within the population.}$$

Claim 73 (currently amended): The program storage device of claim 52, wherein

$I(DF_1, DF_2) = H(DF_2) * E(DF_2) / (1 + \exp((DF_1 - a)/b))$, and wherein DF_1 is a ~~type 1 diabetes feature that~~ represents an incidence of type 1 diabetes for the virtual patient so that values of DF_1 above a first threshold value correspond to an occurrence of type 1 diabetes in the virtual patient, DF_2 is a ~~type 2 diabetes feature that~~ represents an incidence of type 2 diabetes for the virtual patient so that values of DF_2 above a second threshold value correspond to an occurrence of type 2 diabetes in the virtual patient, H represents a degree of insulin resistance in a person with diabetes, and the parameters a and b are set to fit data for I , DF_1 and DF_2 for a population that is represented by the virtual patient.

Claim 74 (previously presented): The program storage device of claim 52, wherein the at least one value based on the virtual patient's FPG at time t is saved to a computer-readable medium.

Claim 75 (previously presented): The program storage device of claim 66, wherein the method further comprises:

setting values for the parameters a , b , c , and d by fitting the equation representing E to data for the population according to a least-squares criterion.

Claim 76 (new): The method of claim 1, wherein the virtual patient's FPG corresponds to a steady-state level of glucose after fasting by the virtual patient.

Claim 77 (new): The method of claim 3, wherein DF_2 reaches the threshold value at a time corresponding to an age of the virtual patient when the symptoms of type 2 diabetes first occur.

Claim 78 (new): The apparatus of claim 31, wherein the virtual patient's FPG corresponds to a steady-state level of glucose after fasting by the virtual patient.

Claim 79 (new): The apparatus of claim 33, wherein DF_2 reaches the threshold value at a time corresponding to an age of the virtual patient when the symptoms of type 2 diabetes first occur.

Claim 80 (new): The program storage device of claim 52, wherein the virtual patient's FPG corresponds to a steady-state level of glucose after fasting by the virtual patient.

Claim 81 (new): The program storage device of claim 66, wherein DF_2 reaches the threshold value at a time corresponding to an age of the virtual patient when the symptoms of type 2 diabetes first occur.